PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference MJL-VB60298	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/EP2004/006426	International filing date *(day/month/year)* 14.06.2004	Priority date *(day/month/year)* 16.06.2003
International Patent Classification (IPC) or both national classification and IPC INV. A61K39/102 A61K39/385 A61K39/39 A61P31/04 A61K9/51		
Applicant GLAXOSMITHKLINE BIOLOGICALS S.A. et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 8 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 8 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
18.03.2005	11.05.2006
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Lechner, O Telephone No. +49 89 2399-8687

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP2004/006426

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-32 as originally filed

Claims, Numbers

1-54 received on 15.03.2006 with letter of 15.03.2006

Drawings, Sheets

1/6-6/6 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).

   ☐ the language of publication of the international application (under Rule 48.3(b)).

   ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   ☐ contained in the international application in written form.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority in written form.

   ☐ furnished subsequently to this Authority in computer readable form.

   ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   ☐ the description, pages:

   ☒ the claims, Nos.: 55-59

   ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

   ☐ the entire international application,

   ☒ claims Nos. 30, 44, 45 (in part), 37

   because:

   ☒ the said international application, or the said claims Nos. 30, 44, 45 (in part) relate to the following subject matter which does not require an international preliminary examination (specify):

   see separate sheet

   ☒ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. 37 are so unclear that no meaningful opinion could be formed *(specify)*:

   see separate sheet

   ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

   ☐ no international search report has been established for the said claims Nos.

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

   ☐ the written form has not been furnished or does not comply with the Standard.

   ☐ the computer readable form has not been furnished or does not comply with the Standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	5-9, 11, 13, 20-33, 37-48, 51-57
	No:	Claims	1-4, 10, 12, 14-19, 34-36, 49, 50, 58, 59
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-59
Industrial applicability (IA)	Yes:	Claims	1-34, 36-48, 51-59
	No:	Claims	

2. Citations and explanations

see separate sheet

Item III

1. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability (Rule 67.1, PCT)

Claims 30, 44, 45 relate to subject matter considered by this Authority to be covered by the provisions of **Rule 67.1(iv), PCT**. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject matter of these claims **(Article 34(4)(a)(I), PCT)**.

Item V

1 The following prior art documents have been mentioned during the procedure:

D3 WO 98/17310 A (DIMMINACO AG S A LTD ; HILGERS LUUK (NL)) 30 April 1998 (1998-04-30)

D9 DIWAN MANISH ET AL: "Enhancement of immune responses by co-delivery of a CpG oligodeoxynucleotide and tetanus toxoid in biodegradable nanospheres." JOURNAL OF CONTROLLED RELEASE, vol. 85, no. 1-3, 13 December 2002 (2002-12-13), pages 247-262, XP004397783 ISSN: 0168-3659

D10 von Hunolstein-C et al: "The adjuvant effect of synthetic oligodeoxynucleotide containing CpG motif converts the anti-Haemophilus influenzae type b glycoconjugates into efficient anti-polysaccharide and anti-carrier polyvalent vaccines" Vaccine. 2001 Apr 30;19(23-24):3058-66. XP4234176

D11 Payne-LG et al: "PCPP as a parenteral adjuvant for diverse antigens. Dev Biol Stand. 1998;92:79-87. XP009040091

D12 Watson-DL et al. "Influence of adjuvants on the immune response of sheep to a novel Staphylococcus aureus vaccine" Veterinary Microbiology 34 (1993) 139-153 XP001059709

D13 Sánchez-A et al: "Formulation strategies for the stabilization of tetanus toxoid in poly(lactide-co-glycolide) microspheres. Internat. J. Pharmaceutics 1999, 185:255-266

2 Novelty (Article 33(2), PCT)

2.1 It would appear that no documents are comprised in the available prior art disclosing an immunogenic composition comprising a capsular polysaccharide or oligosaccharide of Haemophilus influenzae B (PRP), and a polyanionic polymer, wherein the polyanionic polymer is an oligo- or poly-peptide and comprises anionic constitutional repeating units obtained from a group consisting of: L-aspartic acid, D-aspartic acid, L-glutamic acid, D-glutamic acid, and salts of the foregoing, and which has a monomer content of not less than 30, 40, 50, 60, 70, 80, 90 or 100% L-aspartic acid and/or L-glutamic acid. It would

also appear that no documents are comprised in the available prior art disclosing a method for reducing immunological interference of Haemophilus influenzae B capsular polysaccharide or oligosaccharide characterized by the steps of 1) adsorbing the one or more further antigens onto the adjuvant; 2) adding a polyanionic polymer to said one or more further antigens; and 3) then adding an immunogenic composition comprising PRP to said one or more further antigens

Thus, the subject matter of **claims 1-54** has to be considered novel (**Art. 33(2), PCT**).

3 Inventive step (Article 33(3), PCT)

D11 is considered to represent the closest prior art document and analyses the adjuvanticity of the phosphazene polymer *(polyanionic polymer)*, poly[di(carboxylatophenoxy) phosphazene (PCPP) with a diverse collection of immunogens. PCPP is shown to be a potent adjuvant for capsular polysaccharides PRP from Haemophilus influenzae type b. PCPP is a superior adjuvant at least with TT compared to similar negatively charged polyanions, polymethylacrylic and polyacrylic acid (c.f. abstract; p 84-86).

3.1 claims 2-31, 44-54

The subject matter of **claim 1** differs from **D11** in that it discloses immunogenic compositions comprising an alternative polyanionic polymer, wherein the polyanionic polymer is an oligo- or poly-peptide and comprises anionic constitutional repeating units obtained from a group consisting of: L-aspartic acid, D-aspartic acid, L-glutamic acid, D-glutamic acid, and salts of the foregoing, and which has a monomer content of not less than 30, 40, 50, 60, 70, 80, 90 or 100% L-aspartic acid and/or L-glutamic acid.

The application provides evidence that I) poly-L-glutamate avoids flocculation induced by PRP-T (c.f. example 1, p 20), ii) the presence of poly-l-glutamate in Hib formulations reduces immune interference observed with combinations of Hib and Infanrix-Penta combinations (c.f. Fig. 4; p 23, 24) resulting in high anti-PRP Ab titres; iii) the Hib response after vaccination with DTPa-HBV-IPV/HibPLG is significantly higher as compared to DTPa-HBV-IPV/Hib (c.f. p 31, 32)

Therefore, the technical problem is to provide alternative polyanionic polymers for microencapsulation of Hib.

The claimed solution is the use polyanionic polymers, wherein the polyanionic polymer is an oligo- or poly-peptide and comprises anionic constitutional repeating units obtained from a group consisting of: L-aspartic acid, D-aspartic acid, L-glutamic acid, D-glutamic acid, and salts of the foregoing, and which has a monomer content of not less than 30, 40, 50, 60, 70,

80, 90 or 100% L-aspartic acid and/or L-glutamic acid.

Starting from the closest prior art alone, a skilled person would be aware, that a variety of different polyanionic polymers can be used in order to prepare alternative immunogenic formulations (c.f. e.g. **D3**, **D12** or **D13**).
However, the skilled person would have no indication that formulation of Hib (PRP) with polyanionic glutamate/aspartate oligo- or polypeptide polymers drastically reduces immune interference observed when combining Hib with other vaccines resulting in significantly higher Hib responses after vaccination (c.f. p 31, 32).
Thus, the subject matter of **claim 1** and consequently also of **claims 2-54** would appear to involve an inventive step in the sense of **Art. 33(3), PCT**.

4 further remarks

4.1 Contrary to the requirements of **Rule 5.1(a)(ii), PCT**, the relevant background art disclosed in **D9-D12**, would not appear to be mentioned/discussed in the description, nor are these documents identified therein (**Guidelines 4.05**).

4.2 It would appear, that none of the experiments provided in the application use the claimed method. *Example 1* provides data on Hib-PLG formulations; *Example 2* analyses the effect of flocculation/aggregation in Infanrix, Tritanix formulations; *Example 3* provides data from a phase II clinical trial showing that DTPa-HBV-IPV (licensed formulation - i.e. not microencapsulated with polyanionic polymers) + Hib-TT-PLG results in a slightly higher (protective) response compared to DTPa-HBV-IPV/Hib or DTPa-HBV-IPV and Hiberix, respectively.
Thus, **claims 32-43** would appear to lack support in the sense of **Art. 6, PCT**.

4.3 The vague statements in the description on p 19, l 31 imply that the subject-matter for which protection is sought may be different to that defined by the claims, thereby resulting in lack of clarity (**Article 6, PCT**) when used to interpret them.

4.4 Expressions like "preferably", "for example", "such as" or "more particularly" are considered to have no limiting effect on the scope of the claim (c.f. **claim 4, 9, 12, 13, 15, 20, 28, 32, 34, 38, 44, 46, 48**); that is to say, the feature following any such expression is to be regarded as entirely optional (c.f. **Guidelines 5.40**).

4.5 The scope of **claims 29-31** relating to a therapeutic use of the compositions of **claims 1-28** also comprises salts of anionic constitutional repeating units (c.f. e.g. **claim 1**) which are not suitable for pharmaceutical use.

4.6 The repeated use of the non restrictive term/phrase "about", "around" or similar terms

introduces ambiguity into **claims 9, 13** (c.f. **PCT Guidelines, Section IV, III-4.5a**).

Claims

We claim:

1. An immunogenic composition comprising a capsular polysaccharide or oligosaccharide of *Haemophilus influenzae* B (PRP), and a polyanionic polymer, wherein the polyanionic polymer is an oligo- or poly-peptide and comprises anionic constitutional repeating units obtained from a group consisting of: L-aspartic acid, D-aspartic acid, L-glutamic acid, D-glutamic acid, and salts of the foregoing, and which has a monomer content of no less than 30, 40, 50, 60, 70, 80, 90 or 100% L-aspartic acid and/or L-glutamic acid.

2. The immunogenic composition of claim 1, wherein PRP is conjugated to a carrier protein which is a source of T-helper cell epitopes.

3. The immunogenic composition of claim 2, wherein the carrier protein is selected from the group consisting of: tetanus toxoid, diphtheria toxoid, CRM197, and protein D.

4. The immunogenic composition of claims 1-3, wherein the oligo- or polypeptide consists of, on average, 4-200 or 5-200 residues, preferably 8-117 residues, more preferably 15-18 residues, most preferably 17 residues.

5. The immunogenic composition of claims 1-4, wherein the polyanionic polymer is polyanionic heteropolymer.

6. The immunogenic composition of claim 5, wherein the polyanionic heteropolymer consists of two distinct anionic constitutional repeating units.

7. The immunogenic composition of claims 1-4, wherein the polyanionic polymer is a polyanionic homopolymer.

8. The immunogenic composition of claim 7, wherein the polyanionic polymer is poly-L-glutamic acid (PLG).

9. The immunogenic composition of claims 1-8, wherein the result of multiplying the concentration of the polyanionic polymer (in μM) by the net negative charge of the polyanionic polymer at pH 7.0 divided by the amount of PRP present in a 0.5 mL dose of the immunogenic composition (in μg) is 300-6000, preferably 400-4000, more preferably 500-2000, 560-1100, 610-900, 640-800, or 660-700, and most preferably around or exactly 680.

10. The immunogenic composition of claims 1-9, wherein the concentration of the polyanionic polymer in the composition is 30-2000 in μM.

11. The immunogenic composition of claims 1-10, wherein the polyanionic polymer has a net negative charge at pH 7.0, on average, of at least 8, and preferably at least 17.

12. The immunogenic composition of claims 1-11, wherein the polyanionic polymer has at least on average 1 net negative charge at pH 7.0 per 3 monomers, preferably at least 2 per 3 monomers, and most preferably at least on average 1 net negative charge for each monomer.

13. The immunogenic composition of claims 1-12, wherein the amount of PRP present in a 0.5 mL dose of the immunogenic composition is 1-20, preferably 2.5-10, and most preferably around or exactly 5 μg.

14. The immunogenic composition of claims 1-13, wherein the immunogenic composition comprises one or more further antigens.

15. The immunogenic composition of claim 14, wherein the one or more further antigens comprise one or more meningococcal capsular oligosaccharide or polysaccharide – carrier protein conjugates selected from a group consisting of: MenC, MenY, MenA and MenW, preferably MenC and/or MenY.

16. The immunogenic composition of claim 14 or 15, wherein the one or more further antigens comprise one or more pneumococcal capsular oligosaccharide or polysaccharide – carrier protein conjugates.

17. The immunogenic composition of claim 15 or 16, wherein the carrier protein is selected from the group consisting of: tetanus toxoid, diphtheria toxoid, CRM197, and protein D.

18. The immunogenic composition of claims 14-17, wherein the one or more further antigens comprise tetanus toxoid, diphtheria toxoid, and inactivated whole-cell *B. pertussis* or one or more acellular *B. pertussis* antigens.

19. The immunogenic composition of claims 14-18, wherein the one or more further antigens comprise one or more acellular *B. pertussis* antigens selected from the group consisting of: pertussis toxiod, FHA, pertactin, agglutinogen 2 and agglutinogen 3.

20. The immunogenic composition of claims 14-19, wherein the one or more further antigens comprise either or both of Inactivated Polio Vaccine (IPV) and Hepatitis B surface antigen, wherein Hepatitis B surface antigen is preferably adsorbed onto aluminium phosphate.

21. The immunogenic composition of claims 14-20, which further comprises an adjuvant with a zero point charge greater than 8; wherein the polyanionic polymer prevents flocculation between the adjuvant and PRP and/or reduces the immunological interference that the adjuvant has on PRP.

22. The immunogenic composition of claim 21, wherein the adjuvant is selected from the group consisting of: alum and aluminium hydroxide.

23. The immunogenic composition of claim 21 or 22, wherein the adjuvant is present in the immunogenic composition in the amount of 100-1000 μg per 0.5 mL dose.

24. The immunogenic composition of claims 21-23, wherein at least one of the one or more further antigens is adsorbed onto the adjuvant.

25. The immunogenic composition of claim 24, wherein the presence of the polyanionic polymer does not cause significant desorption of the one or more further antigens adsorbed onto the adjuvant.

26. The immunogenic composition of claim 24 or 25, comprising the following antigens adsorbed onto aluminium hydroxide: diphtheria toxoid, tetanus toxoid, pertussis toxoid, FHA and pertactin.

27. The immunogenic composition of claim 26, further comprising unadsorbed IPV and/or Hepatitis B surface antigen adsorbed onto aluminium phosphate.

28. The immunogenic composition of claims 1-27, which is lyophilised and further comprises a stabilizing excipient selected from the group consisting of: glucose, maltulose, iso-maltulose, lactulose, sucrose, sorbitol, maltose, lactose, iso-maltose, maltitol, lactitol, palatinit, trehalose, raffinose, stachyose, and melezitose; preferably sucrose.

29. A vaccine comprising the immunogenic composition of claims 1-28 and a pharmaceutically acceptable excipient.

30. A method of preventing or treating *H. influenzae* B disease comprising the steps of administering a pharmaceutically effective amount of the vaccine of claim 29 to a patient in need thereof.

31. The use of the immunogenic composition of claims 1-28 or the vaccine of claim 29 in the manufacture of a medicament for the prevention or treatment of *H. influenzae* B disease.

32. A method to reduce the immunological interference of a *Haemophilus influenzae* B capsular polysaccharide or oligosaccharide (PRP), preferably

conjugated, in a combination vaccine comprising one or more further antigens adsorbed to an adjuvant with a zero point charge greater than 8, wherein such method comprises the steps of:

(i) adsorbing the one or more further antigens onto the adjuvant;

(ii) adding a polyanionic polymer to said one or more further antigens, wherein the polyanionic polymer is an oligo- or poly-peptide and comprises anionic constitutional repeating units obtained from a group consisting of: L-aspartic acid, D-aspartic acid, L-glutamic acid, D-glutamic acid, and salts of the foregoing, and which has a monomer content of no less than 30, 40, 50, 60, 70, 80, 90 or 100% L-aspartic acid and/or L-glutamic acid; and

(iii) then adding an immunogenic composition comprising PRP to said one or more further antigens.

33. The method of claim 32, wherein the combination vaccine is the immunogenic composition of any one of claims 21-27.

34. A method to reduce the immunological interference of a *Haemophilus influenzae* B capsular polysaccharide or oligosaccharide (PRP), preferably conjugated, in a combination vaccine comprising one or more further antigens adsorbed to an adjuvant with a zero point charge greater than 8, wherein such method comprises the steps of:

(i) adsorbing the one or more further antigens onto the adjuvant; and

(ii) adding an immunogenic composition comprising PRP and a polyanionic polymer to said one or more further antigens, wherein the polyanionic polymer is an oligo- or poly-peptide and comprises anionic constitutional repeating units obtained from a group consisting of: L-aspartic acid, D-aspartic acid, L-glutamic acid, D-glutamic acid, and salts of the foregoing, and which has a monomer content of no less than 30, 40, 50, 60, 70, 80, 90 or 100% L-aspartic acid and/or L-glutamic acid.

35. The method of claim 34, wherein the immunogenic composition is that of any one of claims 1-13.

36. The method of claim 34 or 35, wherein the combination vaccine is the immunogenic composition of any one of claims 21-27.

37. The method of any one of claims 32-36 wherein the immunogenic composition is added extemporaneously to said one or more further antigens.

38. The method of claims 32-34, wherein the immunogenic composition is lyophilised in the presence of a stabilizing excipient selected from the group consisting of: glucose, maltulose, iso-maltulose, lactulose, sucrose, sorbitol, maltose, lactose, iso-maltose, maltitol, lactitol, palatinit, trehalose, raffinose, stachyose, and melezitose; preferably sucrose.

39. The method of claims 32-38, wherein the immunogenic composition further comprises one or more conjugated meningococcal capsular oligosaccharides or polysaccharides selected from a group consisting of: MenC, MenY, MenA and MenW, preferably MenC and/or MenY.

40. The method of claims 32-39, wherein the immunogenic composition further comprises one or more conjugated pneumococcal capsular oligosaccharides or polysaccharides.

41. The method of claims 32-40, wherein the adjuvant is aluminium hydroxide.

42. The method of claims 32-39, wherein the one or more further antigens comprise the following antigens: diphtheria toxoid, tetanus toxoid, pertussis toxoid, FHA and pertactin.

43. The method of claims 32-40, wherein the presence of the polyanionic polymer in the combination vaccine does not cause significant desorption of the one or more further antigens adsorbed to the adjuvant.

44. The use of a polyanionic polymer in an immunogenic composition further comprising a *Haemophilus influenzae* B capsular polysaccharide or oligosaccharide (PRP), preferably conjugated, as a means for protecting the immune response of PRP,

wherein the polyanionic polymer is an oligo- or poly-peptide and comprises anionic constitutional repeating units obtained from a group consisting of: L-aspartic acid, D-aspartic acid, L-glutamic acid, D-glutamic acid, and salts of the foregoing, and which has a monomer content of no less than 30, 40, 50, 60, 70, 80, 90 or 100% L-aspartic acid and/or L-glutamic acid.

45. The use of claim 44, wherein the immunogenic composition is that of claims 1-28.

46. A kit comprising: i) a first immunogenic composition comprising a *Haemophilus influenzae* B capsular polysaccharide or oligosaccharide (PRP), preferably conjugated, and a polyanionic polymer, wherein the polyanionic polymer is an oligo- or poly-peptide and comprises anionic constitutional repeating units obtained from a group consisting of: L-aspartic acid, D-aspartic acid, L-glutamic acid, D-glutamic acid, and salts of the foregoing, and which has a monomer content of no less than 30, 40, 50, 60, 70, 80, 90 or 100% L-aspartic acid and/or L-glutamic acid; and ii) a second immunogenic composition comprising one or more antigens adsorbed onto an adjuvant with a zero point charge greater than 8.

47. The kit of claim 46, wherein the first immunogenic composition is the immunogenic composition of claims 1-20.

48. The kit of claim 46 or 47, wherein the first immunogenic composition is lyophilised and further comprises a stabilizing excipient, preferably sucrose, and the second immunogenic composition is liquid.

49. The kit of claims 46-48, wherein the first immunogenic composition further comprises one or more conjugated meningococcal capsular oligosaccharides or polysaccharides selected from a group consisting of: MenC, MenY, MenA and MenW, preferably MenC and/or MenY.

50. The kit of claims 46-49, wherein the first immunogenic composition further comprises one or more conjugated pneumococcal capsular oligosaccharides or polysaccharides.

51. The kit of claims 46-50, wherein the adjuvant is aluminium hydroxide.

52. The kit of claims 46-51, wherein the second immunogenic composition comprises one or more antigens selected from a group consisting of: diphtheria toxoid, tetanus toxoid, pertussis toxoid, FHA and pertactin.

53. The use of a polyanionic polymer in the manufacture of an immunogenic composition for the prevention of aggregation or flocculation occurring in said composition, wherein the polyanionic polymer is an oligo- or poly-peptide and comprises anionic constitutional repeating units obtained from a group consisting of: L-aspartic acid, D-aspartic acid, L-glutamic acid, D-glutamic acid, and salts of the foregoing, and which has a monomer content of no less than 30, 40, 50, 60, 70, 80, 90 or 100% L-aspartic acid and/or L-glutamic acid.

54. An immunogenic composition comprising a saccharide antigen with a pI less than 3, and a polyanionic polymer, wherein the polyanionic polymer is an oligo- or poly-peptide and comprises anionic constitutional repeating units obtained from a group consisting of: L-aspartic acid, D-aspartic acid, L-glutamic acid, D-glutamic acid, and salts of the foregoing, and which has a monomer content of no less than 30, 40, 50, 60, 70, 80, 90 or 100% L-aspartic acid and/or L-glutamic acid.